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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/622,776	08/23/00	BURCZAK J	DEX-0079

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EXAMINER	
HOLLERAN, A	
ART UNIT	**PAPER NUMBER**
1642	3

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/622,776	Applicant(s) BURCZAK ET AL.	
	Examiner Anne Holleran	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-15* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-15 are pending and examined on the merits.

Priority

2. The specification lacks a reference, in the first sentence of the application, to the prior filed international application. Amendment of the specification is required.

3. This application claims priority to a continuation-in-part parent, 09/111,938, filed 07/08/1998. The specification and claims of 09/111,938 do not support the full scope of the claims of the instant application because the specification and claims of 09/111,938 describe and are drawn to methods for testing human subjects, while the instant claims are drawn to methods for any subject. Thus, the scope of the claims is broader than what was contemplated in 09/111,938. Thus, for comparison with the prior art, the filing date of 09/175,504 (10/20/1998) will be used.

Claim Rejections - 35 USC § 112

4. Claims 1-5 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the correlation statement does not match with the preamble statement. Claim 1 is drawn to a method of monitoring cancer that has not metastasized for the

onset of metastasis, whereas the correlative statement is directed to determining that one has a metastatic cancer.

Claim 10 is indefinite because the preamble recites a method for diagnosing ovarian or testicular cancer, while the correlative statement is directed to all cancers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1-3, 5 and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Schmidt et al (U.S. Patent 5,747,264; issued May 5, 1998; filed September 16, 1996).

Claims 1-3 and 5 are drawn to methods of monitoring cancer in a patient comprising detecting levels of PLA_2 in a bodily fluid. Claims 13-15 are drawn to methods of monitoring progression, remission, response to therapy and stabilization of prostate, breast, ovarian, or testicular cancer, comprising measuring PLA_2 levels in bodily fluid samples. The bodily fluid may be serum, and the method of measurement may be ELISA.

U.S. patent 5,747,264 discloses methods for diagnosing, monitoring progression, remission or recurrence of prostate cancer (col. 1, line 65 – col. 2, line 8), and teaches that elevated levels of mRNA encoding PLA_2 are present in prostate cancer (col. 1, lines 48-59).

The detection of onset of metastasis is considered to be an obvious species of "monitoring progression", because metastasis is a well known event in the progression of a cancer. A diagnostic assay is also disclosed for the detection of PLA_2 protein in bodily fluids (col. 2, lines 39-42). Among the assay techniques that are taught is the ELISA assay. Thus, U.S. Patent 5,747,264 discloses methods that are the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 2, 5-7, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamashita et al[a] (Yamashita, S. et al., Clin. Chim. Acta, 228: 91-99, 1994; cited in the IDS) in view of Yamashita et al[b] (Yamashita, S. et al., Surgery, 117: 601-608, 1995).

Claims 1, 2, and 5 are drawn to methods of monitoring cancer that has not yet metastasized. Claims 6 and 7 are drawn to method for diagnosing a metastatic cancer and claims 13 and 14 are drawn to methods of monitoring the progression, remission, response to therapy, and stabilization of prostate, breast, ovarian, or testicular cancer. All of the claimed methods comprise measuring PLA_2 levels, wherin an elevated level of PLA_2 is indicative of metastatic cancer, or wherein a decreased PLA_2 level is indicative of a remission or response to therapy, or wherein no change in PLA_2levels is indicative of stabilization of cancer.

Yamashita[a] teaches the meaurement, by radioimmunoassay, of M-PLA_2 levels (which is the same as Group II PLA_2, see page 91 and 92) in serum samples of patients classified as either M0 (without distant metastasis) or N0 (without lymph node involvement) and in patients classified as either M1 (with distant metastasis) or N1(with lymph node involvement). Yamashita[a] teaches that there is a significant difference between patients with and without metastasis for esophagus, stomach, colon, pancreas, bile duct and breast cancer, and thus demonstrates that the measurement of PLA_2 can be used to differentiate between patients with metastasis and those without metastasis (see page 95, Figure 2). Yamashita[a] does not expressly teach the measurement of PLA_2 as part of a method for monitoring patients for metastasis. However, Yamashita[b] teaches that the M-PLA_2 level in breast cancer is an independent prognostic factor in node-negative breast carcinoma (page 606-607). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a method for monitoring the onset of metastasis or for diagnosing metastasis in view of the teachings of Yamashita[a] and Yamashita[b]. One would have been motivated to use the teachings of Yamashita[a] to devise such a method because of a long felt need for methods to differentiate between patients with metastatic cancer from those without metastatic cancer (see Yamashita[b], page 601-602). One would have had a reasonable expectation of success because the number of different cancers that were studied and because Yamashita[a] also teaches that the increase in serum M-PLA_2 levels are due to production and secretion of M-PLA_2 by cancer cells, indicating that increased secretion of PLA_2 is due to an increase in tumor cell number.

7. Claims 1, 3, 6, 8, 10, 12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamashita et al[a] (Yamashita, S. et al., Clin. Chim. Acta, 228: 91-99, 1994; cited in the IDS) in view of Yamashita et al[b] (Yamashita, S. et al., Surgery, 117: 601-608, 1995) and further in view of Roitt et al (Roitt, I.M. et al. Immunology, 3rd ed, Mosby, St. Louis, 1993, page 25.6 and 25.7) or Holme et al (Holme, D.J. et al , Analytical Biochemistry, 2nd Ed. Longman Scientific and Technical, 1993, page 252-255).

Claims 3, 8, 12 and 15 are drawn to methods where the measurement of PLA_2 is by ELISA. Either Roitt or Holme teach both radioimmunoassay and ELISA. The major difference between the two assays is that detection by radioimmunoassay is by detection of bound radioactivity and that detection in ELISA is by detection of chromogen that has been converted to a colored end product by an enzyme bound to an antibody specific for the detected antigen. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the assay of Yamashita[a] using the teachings of either Roitt or Holme to develop an ELISA method instead of a radioimmunoassay method. One would have been motivated to substitute the ELISA method for the radioimmunoassay method in order to avoid the use of radioisotopes, which are known to be hazardous and difficult to dispose of.

Conclusion

Claims 4 and 9 are free of the art. Claim 9 is objected to for depending from a rejected claim. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
October 1, 2001

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